動脈硬化発症の原因となるLDLの酸化的修飾に関する機能分子とその機構の解明

著者	高橋 吉孝
著者別表示	Takahashi Yoshitaka
雑誌名	平成15(2003)年度 科学研究費補助金 基盤研究(C)研究成果報告書概要
巻	2002　2003
ページ	2p.
発行年	2005-04-18
URL	http://doi.org/10.24517/00063707

2003 Fiscal Year Final Research Report Summary

Investigation of the functional molecules and mechanism on the LDL oxidation causing atherosclerosis -essential roles of 12/15-lipoxygenase-

Research Project

Project/Area Number

14570101

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

General medical chemistry

Research Institution

KANAZAWA UNIVERSITY

Principal Investigator

TAKAHASHI Yoshitaka KANAZAWA UNIVERSITY, Graduate School of Medical Science, Lecturer, 大学院・医学系研究科, 講師 (10236333)

Co-Investigator(Kenkyū-buntansha)

YOSHIMOTO Tanihiro KANAZAWA UNIVERSITY, Graduate School of Medical Science, Professor, 大学院・医学系研究科, 教授 (60127876)
MURAKAMI Takashi KANAZAWA UNIVERSITY, Graduate School of Medical Science, Assistant Professor, 大学院・医学系研究科, 助教授 (40210009)

Project Period (FY)

2002 – 2003

Keywords

12 / 15-Lipoxygenase / Macrophage / Oxidized LDL / LDL-receptor-related protein / Cholesteryl ester

Research Abstract

Oxidative modification of LDL is a critical step for the development of atherosclerosis. 12/15-Lipoxygenase highly expressed in macrophages is proposed to play a key role of the LDL oxidation ; however, the mechanism on the oxidation of extracellular LDL by intracellular enzyme was not known. We found that binding of LDL to the LDL-receptor-related protein(LRP), a cell-surface receptor expressed in macrophages, is required for the 12/15-lipoxygenase-mediates LDL oxidation by macrophages. The binding of the LDL to the LRP was found to translocates the cytosolic 12/15-lipoxygenase to the plasma membrane in macrophages and the transloation was required for the LDL oxidation. Furthermore, the cholesteryl ester in the LDL particle was selectively transferred to the plasma membrane of macrophages after binding of LRP. These

results strongly suggest that cholesteryl ester in LDL is oxygenated in the plasma membrane by membrane-associated 12/15-lipoxygenase, transferred back to the LDL particle, and sequential radical chain reaction generates the oxidized LDL which is recognized by scavenger receptor in macrophages leading to the foam cell formation. These findings would be useful for the development of the medicines for this 'common disease with a novel mechanism.

Research Products (17 results)

All | Other

All | Publications

[Publications] Yoshimoto, T, Y.Takahashi: "Arachidonate 12-lipoxygenases"Prostaglandins and Other Lipid Mediators. 68. 245-262 (2002)

[Publications] Takahashi, Y., T.Yoshimoto: "What are the functions of mammalian 8-,12-,and 15-lipoxygenases?"Research Advances in Cancer. 2. 221-229 (2002)

[Publications] Fujita, H., K.Koshida, E.T.Keller, Y.Takahashi, T.Yoshimoto et al.: "Cyclooxygenase-2 promotes prostate cancer progression"Prostate. 53. 232-240 (2002)

[Publications] Yoshimoto, T., Y.Takahashi, T.Kino-shita, T.Sakashita, H.Inoue, T.Tanabe: "Growth stimulation and epidermal growth factor receptor induction in cyclooxygenase-overexpressing human colon carcinoma cells"Advances in Experimental Medicine and Biology. 507. 403-407 (2002)

[Publications] Zhu, H., Y.Takahashi, W.Xu, H.Kawajiri, T.Murakami, et al.: "Low density lipoprotein receptor-related protein-mediated membrane translocation of 12/15-lipoxygenase is required for oxidation of low density lipoprotein by macrophages"Journal of Biological Chemistry. 278. 13350-13355 (2003)

[Publications] Xu, W., Y.Takahashi, T.Iwasaki, H.Hattori, T.Yoshimoto: "LDL receptor-related protein plays an essential role in 12/15-lipoxygenase-mediated LDL oxidation by macrophages"Advances in Experimental Medicine and Biology. 525. 181-184 (2003)

[Publications] 高橋 吉孝, 吉本 谷博: "リポキシゲナーゼ研究最前線-動脈硬化と癌細胞増殖への関与"実験医学 第21巻(羊土社). 1771-1774 (2003)

[Publications] Yamamoto, S., H.Suzuki, N.Ueda, Y.Takahashi, T.Yoshimoto: "Mammalian Lipoxygenase (in The Eicosanoids)"John Wiley & Sons, Ltd. 53-59 (2004)

[Publications] Kadoyama, K., Y.Takahashi, H.Higashida, T.Tanabe, T.Yoshimoto: "Cyclooxygenase-2 stimulates production of amyloid beta-peptide in neuroblastoma x glioma hybrid NG108-15 cells."Biochem Biophys Res Commun.. 281. 483-490 (2001)

[Publications] Xu, W., Y.Takahashi, T.Sakashita, T.Iwasaki, H.Hattori, T.Yoshimoto: "Low density lipoprotein receptor-related protein is required for macrophage-mediated oxidation of low density lipoprotein by 12/15-lipoxygenase."J Biol Chem.. 276. 36454-36459 (2001)

[Publications] Fujita, H., K.Koshida, E.T.Keller, Y.Takahashi, T.Yoshimoto, M.Namiki, A.Mizokami: "Cyclqoxygenase-2 promotes prostate cancer progression."Prostate.. 53. 232-240 (2002)

[Publications] Takahashi.Y., T.Yoshimoto: "What are the functions of mammalian 8-,12-,and 15-lipoxygenases?"Res.Adv.Cancer.. 2. 221-229 (2002)

[Publications] Yoshimoto, T, Y.Takahashi: "Arachidonate 12-lipoxygenases"Prostaglandins Other Lipid Mediators.. 68. 245-262 (2002)

[Publications] Takahashi, Y., T.Yoshimoto, N.Hoshi, H.Higashida: "12-Lipoxygenase increases neuronal excitability by inhibiting M-type potassium channels."International Congress Series. 1233. 365-369 (2002)

[Publications] Yoshimoto, T., Y.Takahashi, T.Kinoshita, T.Sakashita, H.Inoue, T.Tanabe: "Growth stimulation and epidermal growth factor receptor induction in cyclooxygenase-overexpressing human colon carcinoma cells."Adv.Exp.Med.Biol.. 507. 403-407 (2002)

[Publications] Zhu, H., Y.Takahashi, W.Xu, H.Kawajiri, T.Murakami, M.Yamamoto, S.Iseki, T.Iwasaki, H.Hattori, T.Yoshimoto: "Low density lipoprotein receptor-related protein-mediated membrane translocation of 12/15-lipoxygenase is required for oxidation of low density lipoprotein by macrophages."J Biol Chem.. 278. 13350-13355 (2003)

[Publications] Xu, W., Y.Takahashi, T.Iwasaki, H.Hattori, T.Yoshimoto: "LDL receptor-related protein plays an essential role in 12/15-lipoxygenase-mediated LDL oxidation by macrophages."Adv.Exp.Med.Biol.. 525. 181-184 (2003)

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-14570101/145701012003kenkyu_seika_hokoku_

Published: 2005-04-18